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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,308	10/24/2001	M. Parameswara Reddy	2058-181	8198

22471 7590 03/31/2004

PATENT LEGAL DEPARTMENT/A-42-C
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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,308	REDDY ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18 and 20-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18 and 20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Please note: There is a change in Examiner handling prosecution in this case from Maurie Baker to Jon Epperson.

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/29/2003 has been entered. Claims 1-15, 18 and 20-25 were pending. Applicants amended claims 1, 12 and 20 in the 12/29/2003 Response. In addition, Applicants added new claims 26-29 and canceled claims 16-17 and 19. Therefore, claims 1-15, 18 and 20-29 are pending and active in the instant application. An action on the merit follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. The Stolowitz et al. rejection under 35 U.S.C. § 102(b) is withdrawn (in part) as a result of Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 102

3. Claims 1-4, 9-11, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Stolowitz et al. (WO 87/06586).

Stolowitz et al. disclose a method of reacting molecules with amine containing, activated supports (see Abstract). Specifically, amine-containing supports of Stolowitz such as aminopropyl silica gel (see, e.g. Example 1 and also page 3, lines 14-18) read on the claimed solid support having at least one available amino group. These amino groups are activated using N,N--carbonyldiimidazole (CDI) or a related azolide" (see page 3, lines 18-20). These read on the claimed activating compound having the structure Ll -X- L2 where X is a carbonyl and L1 and L 2 are azole rings. Applicant's specifically elected species is disclosed by the reference on page 10, line 5. This reads directly on the instant claims 2-4 and 13-15. The reference discloses reacting the activated supports with amine containing compounds, see page 3, lines 21-26. In Example I of Stolowitz et al., glycine is reacted with an activated support. In addition, Stolowitz et al. disclose reacting the activated support with a short peptide and they further give an example of a di-glycine i.e., a chain of two glycines, which reads on a polypeptide chain (e.g., see page 9, lines 2-4, "the functionalizing reagent is a ... short peptide ... or di-glycine [i.e., contains an amide linkage]"). Glycine reads on the claimed biological molecule having at least one reactive amino group. The activation occurs in methylene chloride with triethylamine added, reading directly on instant claims 9 and 10 (see, e.g. Example 1, lines 8-11). The support is washed after activation, reading on instant claim 18 and newly added claim 21 (see, e.g. Example 1, lines 14-16). The coupling (in

Example I of glycine, lines 16-18) is performed in a sodium carbonate buffer, reading on instant claim 11.

Note that the supports of Stolowitz et al. (i.e. aminopropyl silica gel or controlled pore glass; see page 3, lines 14-18) read on the newly added limitation of "bead" and glycine reads on the newly added limitation of polypeptide, as defined by applicant on page 4, lines 25-26 of the instant specification.

Response to Arguments

4. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "This amendment [claim 1 was amended to include the term polypeptide chains] is believed to obviate the Examiner's basis for rejection in that a polypeptide chain clearly does not include the individual amino acid glycine ... an individual amino acid residue that does not contain an amide linkage, does not fall within this definition of a polypeptide or polypeptide chain" (e.g., see 12/29/2003 Response, pages 11-12).

[2] Applicants argue the term "bead" has been deleted from claim 12 and, as a result, the rejection to claim 12 and its dependent claims should be withdrawn (e.g., see 12/29/2003 Response, page 12, section for claim 12).

[3] Applicants argue that claim 20 is now drawn to a solid support that is selected from the group consisting of cellulose, agarose, etc. and thus Stolowitz et al. does not anticipate the newly amended claim because the reference only encompasses silican and controlled pore glass.

This is not found persuasive for the following reasons:

[1] The Examiner contends that Stolowitz et al. teach polypeptides including polypeptides that contain an amide linkage like glycine-NH-CO-glycine (e.g., see page 9, lines 2-4; see also newly amended rejection) and, as a result, Applicants arguments are moot.

[2-3] The Examiner agrees with Applicants and the rejection with regard to claims 12-15 and 20-21 is hereby withdrawn (e.g., see newly amended 35 U.S.C. § 102 rejection above).

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained (in part).

Claim Rejections - 35 USC § 103

5. Claims 1-6, 9-15, 18, 20-23 and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stolowitz et al. (WO 87/06586) and Milton (US 6,146,833; of record).

The teachings of Stolowitz et al. are set forth *supra* (which is incorporated in its entirety herein by reference). The reference teaches a method of reacting molecules with amine-containing, activated supports that reads on the claimed method.

Stolowitz et al. lack the specific teaching of depositing compounds in a particular area on the support (i.e. using printing). Stolowitz et al. also lack the teaching of a plate or film (e.g., see newly amended claim 12). Stolowitz et al. also lack the teaching of a material selected from the group consisting of cellulose, agarose, polypropylene, polystyrene, polymethacrylate, and nylon (e.g., see claims 20, 27). Stolowitz et al.

also lack the specific teaching of the biological molecule being an oligonucleotide (e.g., see claims 25, 28). Stolowitz et al. also lack the specific teaching of an "organic polymer" as a substrate (e.g., claim 26).

However, the use of printing techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the teachings of Milton (see for example, column 12, lines 24-41; see also column 8, line 33; see also column 11, line 62; see also column 17, line 2). The reference teaches methods for printing compounds to make an array. See Examples 5 and 6 (note this procedure is *referred to in the instant specification,* pages 9 and 10). Milton specifically teaches the immobilization of e.g. oligonucleotides and peptides, see Examples 3-9 of the reference. Milton further teaches the use of a plate and a film (e.g., see figures 1-7; see also column 2, lines 5-8 wherein glass slides, polymer films, silicon wafers are disclosed; see also column 2, lines 47-50; see also column 3, line 4; see especially claim 23, "the solid support provided is a film"). In addition, Milton teaches polypropylene, which is an organic polymer (e.g., see column 2, line 5; see also figures 1, 6, 10, 14; see also Examples; see also claims 2, 4, 8 and 11).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al. for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by Milton. One of ordinary skill would have been motivated to do so in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as

taught by Milton. One of ordinary skill would have had a high expectation of success as these printing techniques were well established in the art at the time of filing especially on glass substrates that can withstand harsh conditions (e.g., see Milton, column 2, lines 5-10).

6. Claims 1-15, 18 and 20-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stolowitz et al. (WO 87/06586) and Milton (US 6,146,833; of record) and Okamoto et al. (US 6,476,215) and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465).

The teachings of Stolowitz et al. are set forth *supra* (which are incorporated in their entirety herein by reference). The reference teaches a method of reacting molecules with amine-containing, activated supports that reads on the claimed method.

Stolowitz et al. lack the specific teaching of depositing compounds in a particular area on the support (i.e. using printing) and of using a humid chamber.

However, the use of printing or spotting techniques to deposit biological compounds onto solid supports was well established in the art at the time of filing, as evidenced by the teachings of all of Milton, Guo and Okamoto. The references all teach methods for spotting or printing compounds to make an array. See Milton, column 12, lines 24-41 and Examples 5 & 6 (note this procedure is referred to in the instant specification, pages 9 and 10); Guo et al., page 5457, 1st column; and Okamoto et al., columns 1-3.

Moreover, Guo and Okamoto teach using a humid chamber during the attachment of the probes to their arrays. See Guo, page 5457, 1st column; and Okamoto et al., column

18, lines 42-46, for example. This step is used to complete the reaction and/or to incubate the arrays.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al. for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing or spotting to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by any of Milton, Guo and Okamoto. One of ordinary skill would have been motivated to do so due in order to create covalently attached amine bound biomolecules "immobilized at site specific locations" as taught by Milton (for example). Furthermore, it would have also been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a humid chamber to complete the reaction and/or to incubate the arrays once created. These techniques were also well established in the art as taught by Guo and Okamoto. One of ordinary skill would have had a high expectation of success as these printing and reaction techniques were well established in the art at the time of filing especially on glass substrates that can withstand harsh conditions (e.g., see Milton, column 2, lines 5-10; see also Okamoto et al., column 6, lines 31, 38, 67; see also figures 1-2; see also column 12, line 53; see also Guo, Title and abstract).

Response to Arguments

7. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified

from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue that Stolowitz et al. do not teach biological molecules like polypeptides and, as a result, the immobilization of biomolecules as taught by Milton, is directly against the teachings of Stolowitz et al. (e.g., see 12/23/2003 Response, pages 15-16, "[Stolowitz] expressly teaches not attaching these molecules"; see also page 17, paragraph 4).

[2] Applicants argue that the "Stolowitz does not read on claims 12, 20, 26 and 27" (e.g., see 12/23/2003 Response, page 17, paragraph 1).

[3] Applicants argue that there is no motivation to combine the teachings of Stolowitz with the teachings of Milton because the references do not suggest the desirability of the combination. Milton teaches pendant acyl fluoride functionality and that glass slides, silicon wafers and polymer films were difficult to handle and require special handles or holders. Thus, one of ordinary skill would not be motivated to modify Stolowitz by combine the teachings of Milton as Milton teaches the desirability of solid supports with acyl fluoride functionalities (e.g., see 12/23/2003 Response, page 17, paragraphs 3-4).

[4] Applicants argue that there is no suggestion in Milton that solid supports "having at least one amino group" are desirable to attach a biomolecule (e.g., see 12/23/2003 Response, page 17, paragraph 4).

This is not found persuasive for the following reasons:

[1] The Examiner respectfully contends that Applicants are factually mistaken. Stolowitz et al. do teach the immobilization of polypeptides that contain an amide linkage like glycine-NH-(C=O)-glycine (e.g., see page 9, lines 2-4, "the functionalizing reagent is a ... short peptide ... or di-

glycine [i.e., contains an amide linkage]"; see also newly amended rejection) and, as a result, Applicants arguments are moot.

[2] In response to applicant's arguments against the Stolowitz reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the limitations to which Applicants refer (e.g., plates and films in claim 12, polypropylene in claims 20 and 27, and organic polymer in claim 26) are taught by the combined references (see newly amended rejection above).

[3] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a person of skill in the art would have been motivated to combine the references in order to create covalently attached amine bound biomolecules immobilized at "site specific locations." Thus, as stated in the rejection, since Stolowitz et al. teach the claimed attachment chemistry, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the chemistry of Stolowitz et al. for the activation of a amine-containing support for reaction with an amine compound in an array-type format using printing or

spotting to deliver the amine compound (e.g. oligonucleotides or peptides) as taught by any of Milton, Guo and Okamoto for the reasons set forth in the rejection.

Applicants also argue that Milton only provides support for acyl fluoride functionality apparently at the exclusion of all other solid support attachments (e.g., see 12/23/2003 Response, page 17, paragraphs 3-4). The Examiner contends that this interpretation of Milton is too narrow and further fails to appreciate the teachings of Okamoto et al. and Guo et al. For example, Milton states, "Derivatized polypropylene films, glass slides and silicon wafers have been used for the solid support synthesis of oligonucleotides and peptides at site specific locations on the film, slide or wafer. These materials have been fairly successful because the glass, polypropylene and silicon withstand the physical and chemical rigors of the synthesis and hybridization processes" (e.g., see Milton, column 2, lines 5-10). Thus, Applicants narrow assessment of Milton et al. is unwarranted because Milton et al. explicitly states "oligonucloetides and peptides [can successfully be deposited] at site specific locations on the film, slide or wafer" (e.g., see Milton, column 2, lines 7-8), which would encompass the glass substrates disclosed by Stolowitz et al. In addition, both Okamoto et al. and Guo et al. teach that glass substrates can be used (e.g., see Okamoto et al., column 6, lines 31, 38, 67; see also figures 1-2; see also column 12, line 53; see also Guo, Title and abstract).

[4] In response to applicant's arguments against the Milton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Here, the limitation to which

Applicants refer (e.g., at least one amino group) is taught by the combined references (see newly amended rejection above).

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

New Rejections

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-15, 18 and 20-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stolowitz et al. (WO 87/06586) and Milton (US 6,146,833; of record) and Okamoto et al. (US 6,476,215) and Guo et al. (Nuc. Acids Res. 1994, pp. 5456-5465) and Ekins et al. (Ekins, R. and Chu, F. "Microarrays: their origins and applications" TIBTECH June 1999, 17, 217-218).

For ***claims 1-15, 18 and 20-28***, The combined teachings of Stolowitz et al., Milton, Okamoto et al. and Guo et al teaches all the limitations stated in the 35 U.S.C. 103(a) rejection above (incorporated in its entirety herein by reference), which renders obvious claims 1-15, 18, 20-28.

The combined teachings of Stolowitz et al., Milton, Okamoto et al. and Guo et al. differ from the claimed invention as follows:

For ***claim 29***, the prior art combined teachings of Stolowitz et al., Milton, Okamoto et al. and Guo et al differ from the claimed invention by not specifically reciting the use of hormones, therapeutic drugs or drugs of abuse.

However, Ekins et al teaches the following limitations that are deficient in the combined teachings of Stolowitz et al., Milton, Okamoto et al. and Guo et al:

For ***claim 29***, Ekins et al (see entire document) teaches steroid hormones can be used in microarrays with spotting techniques (see Ekins et al, page 217, middle column, paragraph 3; see also column 3, paragraphs 2-4).

It would have been obvious to one skilled in the art at the time the invention was made to use the spotted arrays with at least one reactive amino group as taught by the combined teachings of Stolowitz et al., Milton, Okamoto et al. and Guo et al with the "steroid hormones" as taught by Ekins et al because Ekins et al teaches that spotted micro arrays can be extended to small molecules including hormones. Furthermore, one of ordinary skill in the art would have been motivated to use "steroid hormones" because Ekins et al explicitly states that hormones can be used for this purpose and that Ink-jet spotting techniques can provide for low-cost manufacturing on an industrial scale using

smaller amounts of binding agent (e.g., see Ekins et al, page 217, columns 2-3). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Ekins et al. explicitly states that microspotting can be used with steroid hormones (e.g., see Ekins et al, page 217, columns 2-3).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
March 29, 2004

BENNETT CELSA
PRIMARY EXAMINER